

In the Claims:

Please cancel claims 1-6, 9 and 16-21 without prejudice.

Please amend the claims as follows:

Claims 1-6 and 16-21 (Cancelled)

7. (Currently Amended) A method for detecting a cellular proliferative disorder in a subject comprising:

- a) contacting a nucleic acid-containing specimen from the subject with an agent that provides a determination of the methylation state of ~~at least one gene or associated regulatory region of the gene selected from MICP1-42 of Table 1 and combinations thereof~~ ppENK; and
- b) identifying aberrant methylation of regions of the gene or regulatory region, wherein aberrant methylation is identified as being different when compared to the same regions of the gene or associated regulatory region in a subject not having said cellular proliferative, thereby detecting a cellular proliferative disorder in the subject.

8. (Original) The method of claim 7, wherein the regions of said gene are contained within CpG rich regions.

9. (Cancelled)

10. (Original) The method of claim 7, wherein aberrant methylation comprises hypermethylation when compared to the same regions of the gene or associated regulatory regions in a subject not having the cellular proliferative disorder.

11. (Original) The method of claim 10, wherein the regions comprise regulatory regions of the gene.
12. (Original) The method of claim 7, wherein the agent is a pair of primers that hybridize with a target sequence in the gene or associated regulatory region of the gene.
13. (Original) The method of claim 7, wherein the nucleic acid-containing specimen comprises a tissue selected from the group consisting of brain, colon, urogenital, lung, renal, prostate, pancreas, liver, esophagus, stomach, hematopoietic, breast, thymus, testis, ovarian, and uterine.
14. (Original) The method of claim 7, wherein the nucleic acid-containing specimen is selected from the group consisting of serum, urine, saliva, blood, duodenal fluid, pancreatic fluid, cerebrospinal fluid, pleural fluid, ascites fluid, sputum, stool, and biopsy sample.
15. (Currently Amended) The method of claim ~~11~~7, wherein said cellular proliferative disorder is selected from the group consisting of low grade astrocytoma, anaplastic astrocytoma, glioblastoma, medulloblastoma, gastric cancer, colorectal cancer, colorectal adenoma, acute myelogenous leukemia, lung cancer, renal cancer, leukemia, breast cancer, prostate cancer, pancreatic cancer, endometrial cancer and neuroblastoma.

Please add the following new claims:

--22. (New) The method of claim 12, wherein the primers pairs are selected from

5'-TTGTGTGGGGAGTTATTGAGT-3' (SEQ ID NO:115);

5'-CACCTTCACAAAAAAAATCAATC-3' (SEQ ID NO:116); and

5'-TGTGGGGAGTTATCGAGC-3' (SEQ ID NO:117);

5'-GCCTTCGCGAAAAAAAATCG-3' (SEQ ID NO:118).

23. (New) The method of claim 7, wherein the cellular proliferative disorder is pancreatic cancer.--

RESTRICTION REQUIREMENT

In response to the Requirement for Restriction dated May 22, 2003, Applicants elect, with traverse, Group II, claims 7-15, drawn to a method for detecting a cellular proliferation disorder, classified in class 435, subclass 6. Applicants further elect the human preproenkephalin A gene for examination (SEQ ID NO: 8 (MICP9 in Table 1)) (see Figure 6b, ppENK; GenBank Accession # X00187 (copy enclosed)). Applicants respectfully traverse the requirement for election of specific primer pairs. One of skill in the art could easily identify unmethylated and methylated sequence primers given the short nucleic acid sequence of ppENK provided in SEQ ID NO:8 or in the public databases (e.g., GenBank). However, in order to be completely responsive, Applicants will elect primers for amplification of ppENK for initial examination purposes only, including the following derived from SEQ ID NO:8:

unmethylated

sense: 5'-TTGTGTGGGGAGTTATTGAGT-3' (SEQ ID NO:115)

antisense: 5'-CACCTTCACAAAAAAAATCAATC-3' (SEQ ID NO:116)

methylated

sense: 5'-TGTGGGGAGTTATCGAGC-3' (SEQ ID NO:117)

antisense: 5'-GCCTTCGCGAAAAAAATCG-3' (SEQ ID NO:118)

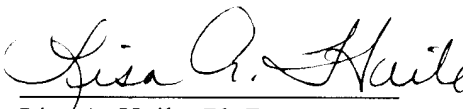
Applicant notes that the product sizes of the ppENK gene in methylation specific PCR (MSP) analysis are as follows: Methylated - 96bp and Unmethylated-100bp. Applicants respectfully request that upon allowance of ppENK and primers SEQ ID NO:115-118, the genus of all primers for amplification of ppENK be rejoined to the allowed claims.

CONCLUSION

Applicants enclose a Petition for an Extension of Time, and a check in the amount of \$465.00 for the extension fee. No further fees are deemed necessary in connection with the filing of this response. However, if any other fee is deemed necessary, the Commissioner is authorized to charge, or apply any credits, to Deposit Account 50-1355. The Examiner is invited to contact Applicants' undersigned representative at (858) 677-1456, if there are any questions related to this matter.

Respectfully submitted,

Date: July 31, 2003



Lisa A. Haile, Ph.D.
Reg. No. 38,347

GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1100
San Diego, CA 92121-2133
USPTO Customer Number 28213